

Amendment to the Specification:

Replace the paragraph at page 30, line 19 to page 31, line 18 with the following amended replacement paragraph:

--Because the frequency of the nuclear inclusion formation was reduced in the double mutant mice, it was of particular interest to compare cerebellar sections from the B05 *SCA1* transgenic mice with and without expression of *Ube3a* to determine if any of the cellular changes observed in the B05 *SCA1* mice were altered. Histopathologically, the B05/*Ube3a*^(m-/p+) cerebellum had thinning of the molecular layer, Purkinje cell vacuolation and cell bodies displaced from the Purkinje cell layer (Figures 10A through 10H 10I). To ascertain a better view of the subcellular localization of ataxin-1 and dendritic morphology of the Purkinje cells, sections from animals at 9.5, 12.5 and 14.5 weeks were examined using antibodies to ataxin-1 (11NQ) and the Purkinje cell-specific protein calbindin. As was observed by light microscopy, immunofluorescence analysis with the 11NQ antibody confirmed a clear reduction in the appearance of NI in the double mutant animals. While the subcellular localization of ataxin-1 was primarily nuclear and concentrated to the NI in the B05 mice, the distribution of ataxin-1 was much more diffuse in the nucleus with limited staining in the cytoplasm in the double mutant animals. More striking however is the radical loss of dendritic arborization, vacuolation, and severe Purkinje cell heterotopia in the sections from the B05 *SCA1* transgenic mice lacking *Ube3a*^(m-/p+) expression. The striking alterations in Purkinje cell morphology that develop in the double mutant mice at 14.5 weeks are comparable to that of B05 *SCA1* mice at ages greater than 9 months. These results indicate that lack of expression of an E3 ubiquitin ligase accelerates the polyglutamine-induced pathology in the *SCA1* transgenic animals. Additionally, this dramatic pathology is not dependent on NI formation.--